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11 TITLE (Include Security Classification)
(U) Control of Synthetic Peptide Tertiary Structure

12 PERSONAL AUTHOR(S)
Paul B. Hopkins

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16 SUPPLEMENTARY NOTATION

17 COSATI CODES			18 SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
FIELD	GROUP	SUB-GROUP	Peptide secondary structure, molecular design, circular dichroism, α-helix, protein thermostabilization.

19 ABSTRACT (Continue on reverse if necessary and identify by block number)

The proposed research seeks to design and synthesize large organic molecules possessing precisely defined geometric shapes, a capability which will make possible the design of catalysis and receptors. The approach entails the design of unnatural amino acids which, when incorporated into peptides, will enforce tertiary structure on the overall molecule. Methods are also suggested whereby transiently stable noncovalent complexes of peptides might be permanently stabilized by covalent crosslinking, leading to the concept of "self-assembly" of large, highly ordered organic molecules. The additional possibility of assembling large structures from smaller pieces by incorporation of temporary functionality which will initially spatially orient small pieces prior to covalent assembly is suggested, a concept termed "directed assembly."

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89 06 094

Progress Report on Contract N00014-88-K-0201

Principal Investigator: Paul B. Hopkins

Contractor: University of Washington

Contract Title: Control of Synthetic Peptide Tertiary...

Start Date: 1 February 1988

Current Date: 1 July 1989

Research Objective:

The design, synthesis, and structural characterization of peptides of 10 to 35 residues with stable secondary and tertiary structure

Progress (Year 1):

During the report period, we synthesized amino acids bearing side chains possessing metal-ligating functional groups. These residues were incorporated by solid phase techniques into synthetic peptides, and the structures of the peptides were evaluated using circular dichroism in the presence and absence of metals. Disappointingly, although the original design anticipated enhances α-helical character in the presence of metals, no enhanced α-helicity was observed under these conditions.

Workplan (Year 2):

We believe that there is little question that coupling the thermodynamically favorable binding of metals to the coil to helix transition of peptides should provide a mechanism of enhancing α-helix content of peptides. We believe that our failure to achieve this centers on improper selection of the length of the tether linking ligand and peptide. We have focused out attentions on a single metal-binding ligand, and are in the process of synthesizing residues in which the tether length connecting α-carbon and ligand is varied. As we have now done in several cases, we will incorporate these into peptides and evaluate their secondary structures using circular dichroism.

Inventions:

None

Publications:

None

Training Activities:

Mr. James J. Kirchner, a native born American citizen in his third year of graudate school and Mr. Fugiang Ruan, a native born citizen of the Peoples Republic of China in his fourth year of graduate school are working on this project.

Awards/Fellowships:

The PI is an Alfred P. Sloan Fellow (1988-1992) and is recipient of an NIH Research Career Development Award. Fuqiang Ruan is a PRC Scholar